

1 REMARKS

2 Status of the Claims

3 Claims 34-35, 37-40, 42-44, 46, 49-51, 54, 56-58, and 60-61 are pending in the present
4 application, Claims 1-33, 36, 41, 45, 47, 48, 52, 53, and 55 having been previously canceled, and
5 Claim 59 having been canceled herein. Claims 34, 39, 42, 50, 54, 56, 60 and 61 have been amended
6 to more clearly define the invention.

7 Rejections of Claims 34, 35, 37-40, 42-44, 46, 49-51, 54, 56-58, and 60-61 35 U.S.C. § 102

8 The Examiner has rejected Claims 34, 35, 37-40, 42-44, 46, 49-51, 54, 56-58, and 60-61
9 under 35 U.S.C. § 102 as being anticipated by Stern (U.S. Patent No. 5,981,956). The Examiner
10 asserts that Stern discloses each element of applicants' claimed invention. Applicants have amended
11 each independent claim, and as amended such claims distinguish over the cited art for the following
12 reasons.

13 Stern specifically discloses that light collected from the object is dispersed by dichroic beam
14 splitter 108 along different detection paths, such that the dispersed light is directed to detectors 124
15 and 140 (see FIGURE 1 from the Stern patent). Each of applicants' independent claims have been
16 amended to recite that the light is dispersed such that a plurality of images are simultaneously formed
17 *on different portions of a single detector*. Such an embodiment is clearly disclosed in applicants'
18 specification as filed (for example, see FIGURES 3 and 13 in particular, as well as FIGURES 4-7,
19 9A-9B, 11, 14, 18 and 20, and the corresponding text in applicants' specification). Employing a
20 single detector has advantages and requirements not taught or recognized by the prior art, thus the
21 modifications to Stern's configuration to achieve an equivalent would not have been obvious to an
22 artisan of ordinary skill.

23 For example, using a single detector in place of a plurality of detectors enables a more
24 expensive, higher quality detector to be employed. As clearly described in applicants' specification,
25 a time delay integration (TDI) detector represents a particularly preferred type of detector (for
26 example, see applicants' FIGURE 21). Because such a detector acquires image data over time while
27 an object moves relative to the imaging system, more image data can be acquired. Stern does not
28 teach or suggest that any advantage can be obtained by replacing these detectors (126, 130, and 140)
29 with a single detector, thus there is no support for concluding that such a modification would have
30 been obvious.

1 Furthermore, the use of a single detector requires a structural configuration that enables a
2 plurality of images to be simultaneously acquired by a single detector. For example, the specification
3 as filed discloses that in one embodiment:

4 The angle of each dichroic beam splitter is set such that light reflected from it
5 within the corresponding spectral bandwidth for the dichroic beam splitter is
6 focused onto a different region of the detector. Since the present invention
7 uses a narrow field angle in object space along axis 257, perpendicular to the
8 axis of motion, many different spectral bandwidths can be simultaneously
9 imaged onto a single detector. In this manner, each region on the detector may
10 cover a different spectral bandwidth, while light is collected over the same
11 field angle in object space (page36, first paragraph, discussing FIGURE14).

12 Clearly, the structural modifications required to enable a plurality of spectrally dispersed
13 images to be simultaneously generated on different portions of a single detector are not trivial. Stern
14 does not teach or suggest such a structure. While the pending claims are method claims, clearly to
15 implement the step of simultaneously generating a plurality of images on different portions of a
16 single detector, one must be able to produce or acquire a structure that can be used to implement such
17 a step. As Stern does not teach or suggest such a structure, logically Stern cannot teach or suggest
18 such a step.

19 The general element of simultaneously generating a plurality of images on different portions
20 of a single detector is recited in each independent claim as amended (using variations in language;
21 but the essential elements are present in each independent claim). The modifications to the cited art
22 required to achieve a method including an equivalent step are not obvious in view of the teaching of
23 the prior art. It is well accepted that dependent claims must be patentable for at least the same
24 reasons as the claims from which they depend. Accordingly, the rejection of Claims 34, 35, 37-40,
25 42-44, 46, 49-51, 54, 56-58, and 60-61 under 35 U.S.C. § 102 as being anticipated by Stern should be
26 withdrawn.

27 Furthermore, it should be noted that independent Claim 42 recites the step of:

28 *collecting light from said object along a collection path, the light that is collected comprising light*
29 *corresponding to each optical signaling component used to label the plurality of specific features that are*
30 *part of the object, such light having been simultaneously collected*

In other words, the object will include a plurality of specific features, each of which is
uniquely labeled, and light from all of the features is simultaneously collected. In Stern's technique,

1 an array of different features, each of which has been labeled, is sequentially scanned to acquire data
2 corresponding to each feature. In general, the features are polymer sequences that are individually
3 labeled. Significantly, while light from each dye used to label a specific polymer sequence is
4 simultaneously collected, it appears that in Stern's technique each different polymer sequence is
5 scanned individually. So if the array includes 100 different polymer sequences, then 100 sets of data
6 are collected over a period of time. Thus, light from only a single polymer sequence is collected at
7 any one time, even though a plurality of different polymer sequences are part of the array being
8 scanned. The scanning functionality is disclosed in the final paragraph of column 6, as well as
9 elsewhere in Stern's disclosure. Stern simply does not teach or suggest that light from a plurality of
10 different features of an object is simultaneously collected, and that such light can be used to
11 determine whether a specific feature is present on the object. In the context of the present invention,
12 spectral signatures from a plurality of different features on a single object are simultaneously
13 acquired, and the identity of each feature can be determined, even where two different features share
14 a common signaling component.

15 For example, as indicated in applicants' FIGURE 2C, two different optical signaling
16 components, A and B, can be used to uniquely label a plurality of different features, where the
17 spectral signature $3A + B$ (or $A-A-A-B$) corresponds to a first feature, the spectral signature $2A + 2B$
18 (or $A-A-B-B$) corresponds to a second feature, and the spectral signature $A + 3B$ (or $A-B-B-B$)
19 corresponds to a third feature. Significantly, Claim 42 recites a method in which light from each of
20 the three features is simultaneously collected, and the unique spectral signature associated with each
21 different feature can be uniquely identified. Stern clearly discloses that a spectral signature including
22 a plurality of components (i.e., a combination of different colored dyes) can be associated with a
23 specific position in the array (i.e., a specific polymer sequence), but Stern does not teach or suggest
24 that the spectral signatures of a plurality of different polymer sequences can be obtained
25 simultaneously (i.e., without scanning).

26 Furthermore, it is not clear from Stern's disclosure whether Stern's apparatus can distinguish
27 between the three different spectral signatures of FIGURE 2C. Stern's apparatus clearly can detect a
28 spectral signature from a single polymer sequence where the spectral signature includes more than
29 one optical signaling component (i.e., Stern's apparatus could detect a spectral signature comprising
30 $A+B$). However, it is not clear that Stern's apparatus could differentiate the different intensities

1 enabling the three different spectral signatures of FIGURE 2C to be distinguished. Even if Stern's
2 apparatus could differentiate the different spectral signatures of FIGURE 2C, Stern does not teach or
3 suggest that light (i.e. spectral signatures) from a plurality of different polymer sequences (i.e.,
4 features) corresponding to different locations on an object should be simultaneously collected (i.e.,
5 Stern appears to specifically disclose that the features of an object are scanned individually).
6 Claim 42 distinguishes over the cited art for this additional reason.

7 Claims 39 and 50 have been amended to recite an additional aspect of the concepts disclosed
8 in the pending application which further distinguish over Stern. Each claim recites that the step of
9 analyzing comprises:

10 *the step of determining if a multiplex of a spectral signature for each of the plurality of*
11 *different optical signaling components is present in that image, such that the following spectral*
12 *signatures can be differentiated, where A corresponds to a first optical signaling component, and B*
13 *corresponds to a second optical signal component, where light defining all such spectral signatures*
14 *has been simultaneously collected:*

15 (a) *a spectral signature comprising A-A-A-B;*

16 (b) *a spectral signature comprising A-A-B-B; and*

17 (c) *a spectral signature comprising A-B-B-B.*

18 This relates to the discussion above with respect to Claim 42, however, the step of analyzing
19 is emphasized over the step of collecting light from the object. The spectral signatures of
20 subparagraphs (a)-(c) are identical to those illustrated in FIGURE 2C. With respect to the method
21 and apparatus disclosed by Stern, if light from features labeled with the spectral signatures A-A-A-B,
22 A-A-B-B, and A-B-B-B are acquired simultaneously, it is not clear whether Stern's apparatus is
23 physically capable of differentiating the different spectral signatures. For example, assume A=red
24 light, and B=blue light. Clearly, Stern's apparatus can detect a spectral signature A+B (red light is
25 detected by a detector configured to respond only to red light, and blue light is detected by a detector
26 configured to detect only blue light). However, Stern's apparatus is collecting light from only one
27 feature/polymer sequence at a time, thus Stern's detectors need not be able to identify a spatial
28 coordinate from which the red or blue light arose. Stern specifically discloses that photomultiplier
29 tubes be used as detectors. Such devices simply identify a quantity of light received, not a spatial
30

1 coordinate of the light received. Since the position of the stage/optics of Stern's device provides the
2 spatial coordinate information, the detectors need not provide that information as well.

3 However, where two different features are labeled with a common signaling component (i.e.,
4 A-A-B-B and A-B-B-B), and light from features labeled with such spectral signatures is
5 simultaneously acquired, the detector must provide both spatial and intensity information to enable
6 the features labeled with such spectral signals to be distinguished.

7 With respect to Stern's analysis, because each feature is individually scanned, there is no need
8 for the ability to spatially distinguish data from signaling components that are acquired
9 simultaneously (i.e., according to Stern's method, signaling components from only one location are
10 acquired at a time). Even if Stern's apparatus could be used to spatially distinguish signaling
11 components from different features where the light from those features is simultaneously acquired,
12 Stern does not teach or suggest such a step. With respect to determining the intensity of a particular
13 signaling component, even if Stern's apparatus provides such information, Stern does not teach or
14 suggest using *intensity* to distinguish different spectral signatures. Claims 49 and 50 distinguish over
15 the cited art for these additional reasons.

16 Analyzing Signatures Acquired Individually Vs. Analyzing Signatures Acquired Simultaneously

17 It appears that the methods recited by applicants are distinguishable over the technique
18 disclosed by Stern, because Stern acquires the spectral signature of different polymer sequences
19 disposed at different locations on an array individually, whereas applicants' methods acquire the
20 spectral signatures of different features disposed at different locations on an object simultaneously.
21 Those techniques are distinctly different.

22 Applicants' technology enables a plurality of features on an object (such as a cell or planar
23 array) to be labeled with different spectral signatures, where some of the spectral signatures include
24 the same components (i.e., the same colors). Light from all of the features on the object is collected
25 simultaneously, and that light is spectrally dispersed and used to generate a plurality of different
26 images of the object. Those images can be used to determine what spectral signatures are present on
27 the object, enabling the specific features on the object to be identified. Stern's technique can identify
28 spectral signatures of all of the features on an object, however, Stern's technique requires that the
29 light from individual features must be collected individually (the scanning step). Significantly,
30 applicants' technique does not require the scanning step disclosed by Stern, thus the time required to

1 acquire data (i.e., light) from the plurality of features on an object is significantly reduced (thus,
2 applicants' technique enables objects to be analyzed more rapidly).

3 Consider, for example, a Cell #1, which has been labeled at four different locations. Note
4 each location can be considered to be a different feature. FIGURE 3 of the pending application
5 shows six different images of two different cells (violet, indigo, blue, green, yellow, and red images)
6 that have been simultaneously acquired for each cell (by spectrally dispersing light from each cell
7 before imaging and detecting). Each cell includes four different features labeled by different
8 combinations of blue, green, yellow and red optical signaling components. Referring again to Cell #1
9 (cell 300 of FIGURE 3), Location 1 (feature 310) is labeled with blue (C1L1=B), Location 2
10 (feature 308) is labeled with green (C1L2=G), Location 3 (feature 304) is labeled with yellow
11 (C1L3=Y), and Location 4 (feature 306) is labeled with red (C1L4=R). Cell 1 is thus labeled with
12 blue, green, yellow and red, and the ratios of the different colors (blue:green:yellow:red) are: 1:1:1:1.

13 Significantly, applicants' technique collects light from each feature simultaneously. Stern's
14 technique would require each locations/feature to be scanned individually (that is, light from each
15 different feature would need to be acquired individually). The techniques are related, but not
16 identical.

17 Furthermore, if Stern's technique were modified to acquire light from more than one polymer
18 sequence simultaneously, it is not clear that Stern's apparatus would be able to spatially identify
19 different optical signaling components. For example, assume polymer sequence 1 is labeled with
20 blue, green, yellow, and red (PS1=BGYR), and polymer sequence 2 is labeled with blue and red
21 (PS2=BR). Stern's apparatus clearly can be configured to detect blue, green, yellow and red light
22 using four different detectors and filters, such that one detector responds only to blue light, another
23 detector responds only to green light, still another detector responds only to yellow light, and the final
24 detector responds only to red light. However, because Stern relies on the position of the stage to
25 determine the location of the specific polymer sequence, it is not apparent whether Stern's apparatus
26 can distinguish the red light from polymer sequence 1 from the red light of polymer sequence 2, if
27 light from polymer sequence 1 and light from polymer sequence 2 are acquired simultaneously. Note
28 that Stern specifically indicates that the detectors be photomultiplier tubes. Such elements will
29 simply respond to the presence of light, as opposed to providing a spatial coordinate. In other words,
30 it appears that Stern's detectors would simply respond to red light, and not be able to identify from

1 which location the light arose, if light from a plurality of different locations is simultaneously
2 acquired.

3 Accordingly, all of the claims now remaining in the application define patentable subject
4 matter that is neither anticipated nor obvious in view of the prior art cited. The Examiner is thus
5 requested to pass the present application to issue in view of the amendments and the remarks
6 submitted above. If there are any questions that might be addressed by a further telephone interview,
7 the Examiner is invited to telephone the undersigned attorney, at the number listed below.

8
9 Respectfully submitted,

10
11 /michael king/
12 Michael C. King
13 Registration No. 44,832

14 MCK/RMA:elm
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30